

REMARKS

Claims 1-4, 12, 13, 21-33, 35, 36, and 38-76 were pending, and claims 39-74 were withdrawn from consideration, when the Office Action of February 23, 2007, was issued. Claims 39-74 have been cancelled by way of this amendment. The Office rejected claims 1-4, 12, 13, 21-33, 35, 36, 38, 75, and 76 under 35 U.S.C. §§ 112, first and second paragraphs. Reconsideration of the rejections is hereby requested.

I. The Amendments to the Claims

Claims 39-74 have been cancelled for being directed to non-elected subject matter. Claim 36 has been amended to clarify that the first and second peptides of the dimer comprise the same peptide, as supported by the specification at, for example, paragraph [0052]. Claim 77 has been added and is supported by the specification at, for example, paragraph [0096]. No new matter has been added by way of this amendment.

II. The Enablement Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1-4, 12, 13, 21-38, 75, and 76 remain rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the description of the specification. This rejection is respectfully traversed for the reasons set forth below.

The pending claims encompass a limited genus of peptides with specified amino acid length that bind to a specific cell receptor. The specification fully discloses methods to make the claimed peptides via, e.g., peptide synthesis, phage display, and other methods well-known in the art. The level of skill in the art of peptide synthesis and DNA manipulation is high, and those of ordinary skill in the art have the requisite expertise to generate the claimed limited genus of peptides. In addition, the specification describes methods to determine candidate peptide binding specificities with respect to VEGFR-3 using, e.g., VEGFR-3 binding assays (see specification at, e.g., page 42, line 1, through page 53, line 2). Thus, the specification discloses sufficient guidance to enable one of ordinary skill in the art to make and use the invention as claimed.

The Office contends that, while the specification discloses methods of making peptides and methods of determining whether candidate peptides have the requisite activity, the specification fails to teach “how to make any peptide variants with amino acid sequence consisting of 8-100 or 7-100 amino acids in length having these activity” (Office Action of February 23, 2007, page 10). To the contrary, Applicants provide the core amino acid sequence responsible for the biological activity required by the claims. The claims recite the structure of that core attribute of the claimed peptides and allow for a finite number of *conservative* substitution variants of that peptide which retain the claimed activity. Because the sequence required for binding ($X_1X_2X_3X_4X_5X_6X_7X_8$ as defined in the claim) is specified in the claim, the enablement requirement is satisfied for peptides containing additional amino acids. In this regard, the claimed peptide sequence is of a finite length such that a *limited* number of peptides are available and the binding domain of the claimed peptide is short compared to other proteins or peptides. Making peptides within the length maximum recited in the claims entails only routine screening to add additional residues *of any sequence* to the core ($X_1X_2X_3X_4X_5X_6X_7X_8$) structure. The total number of combinations is orders of magnitude smaller than where a large protein of complex structure is contemplated. Screening the resulting peptide to verify that the additional sequence did not interfere with the binding activity conferred by the core peptide is performed quickly using routine techniques, such as those provided in the specification. Experimentation, even if extensive, is not necessarily undue if it is routine in the art. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

The Office continues to misapply the principles of the Federal Circuit’s *Wands* decision. *Id.* The patentee in *Wands* provided taught how to make and screen the claimed hybridomas and presented working examples, thereby satisfying Section 112’s enablement requirement. *Wands*, 858 F.2d at 740. The *Wands* court focused on the direction and guidance provided in the specification relating to how to practice the invention. *Id.* The teaching of how to make and screen hybridomas, coupled with the high level of skill in the art, was sufficient to satisfy Section 112, first paragraph. *Id.* The court noted that, while a considerable amount of work may be required to do the making and screening, if such experimentation is routine, the experimentation is not “undue.” *Id.*

Similar to *Wands*, the invention provides a composition that binds to a specific binding target, with the binding identified using well-known screening methods. The specification teaches how to make the claimed peptides having the core amino acid sequence required by the claims. The specification details screening methods for determining peptide activity, and provides several working examples, similar to the disclosure at issue in *Wands*. Given the high level of skill in the art and the guidance provided by the Applicants to make and use peptides of the invention, a worker of ordinary skill would not be required to undertake undue experimentation to make or use the invention. In this regard, the Office contends that predicting the functional activity and tolerated amino acid changes constitutes undue experimentation. Yet, the making and screening required by the claimed invention (peptide synthesis) is much simpler and faster – more routine -- than the making and screening of hybridomas and antibodies set forth in the facts of *In re Wands*, which the Court said was not undue experimentation.

Because Applicants have taught a worker of ordinary skill in the art to make and use the claimed peptides, with only routine experimentation, the rejection under 35 U.S.C. § 112, first paragraph, enablement, should be withdrawn.

III. The Written Description Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 1-4, 12, 13, 21-38, 75, and 76 remain rejected for alleged lack of written description. Applicants respectfully traverse the rejection.

The Office contends that the specification fails to adequately describe the genus of peptides encompassed by the claims. The application describes several genera of peptides, including peptides of 7-100 amino acids (e.g., 8-25 amino acids), having a specific core amino acid sequence which may contain up to three conservative amino acid substitutions. The claimed peptides defined by $X_1X_2X_3X_4X_5X_6X_7X_8$ is quite small in relation to many chemical and biomolecule claims routinely allowed by the Patent Office in accordance with the Office's Written Description Training Manuals. Indeed, the total number of peptides encompassed by the claims is *orders of magnitude* smaller than large proteins having, e.g., 95% amino acid sequence identity suggested by the training manual

examples. Regarding sequence identity, the Office notes that three conservative mutations within the GYWLTIWG “core sequence” of claim 1 results in 63% identity, which is “far below” the 95% sequence identity suggested by the training manual examples (Office Action of February 23, 2007, page 20). The Office fails to appreciate, however, that the sequence variation is restricted to *conservative* mutations, which are well understood in the art *and* described in the application. The application provides several examples of peptides encompassed by the claims in the Sequence Listing and Table 1 at page 27. Given the small genus of peptides claimed, the specification describes a sufficient number of peptides encompassed by the pending claims to satisfy Section 112.

The Office further contends that, in order to make or synthesize a peptide, the amino acid sequence of the peptide is required, and the application allegedly fails to describe the claimed peptides’ amino acid sequence beyond the core sequence recited in the claims (Office Action of February 23, 2007, page 21). The Office’s statements appear to reiterate its previous contention that, even assuming the $X_1X_2X_3X_4X_5X_6X_7X_8$ is adequately described, the rest of a peptide comprising the core sequence is not adequately described without the remaining amino acid sequence. The Office ignores, however, that Applicants have described the structure associated with function of the claimed peptides. The application demonstrates that short peptides, such as the peptide CGYWLTIWGC, can bind VEGFR-3. By teaching short peptide sequences and describing a genus of such sequences, the Applicants have fulfilled the written description requirement of providing structure generally, and structure associated with function specifically. The application also describes how to make longer peptides that contain the core structure (the “necessary common attributes”), and assay them to confirm that they retain the binding function recited in the claims. The application contemplates that the additional amino acids are optional, and can be any amino acids. Because the written description requirement focuses on the “necessary common attributes” of what is claimed, there is no statutory requirement for describing or defining every additional element or variation that a person of ordinary skill could add to an invention that is described in the application.

With respect to claim 33, the Examiner alleges that the claims encompass any modification to the peptide, including modifications beyond what is disclosed in the

specification, and, therefore, the claim is not adequately described. Again, it appears that the Office requires Applicants to recite any and all possible modifications that increase the half-life of a peptide. The application teaches at paragraph [0051], “[s]tandard pharmaceutical and formulation chemistry is used to achieve such goals, e.g., through glycosylation, pegylation, introduction of non-hydrolyzable bonds, mixing with pharmaceutically acceptable diluents, adjuvants, or carriers, and the like.” Additional description of half-life increasing modifications are found, e.g., pages 32-34 of the specification. The subject matter of claim 33 is sufficiently described to satisfy the requirements of Section 112, first paragraph.

For these reasons, the rejection for lack of written description should be withdrawn.

IV. The New Matter Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn.

The Office maintained its rejection of claims 2 and 23 for allegedly containing new matter. This rejection is respectfully traversed. The Office contends that page 28 of the specification and Table 1 disclose cysteine residues at the N- and C- termini of $X_1X_2X_3X_4X_5X_6X_7X_8$ or CGYWLTIWGC, but the specification fails to describe any other peptide having N- and C-terminal cysteines. The Office failed to consider the disclosure of original claims 2 and 23, which recite the terminal cysteine limitation, and pages 14-15 of the application, which reads as follows:

Preferred peptides are from 6 to 100 amino acids in length, e.g., 6, 7, 8, 9, 10, 11, 12, . . . 97, 98, 99, or 100 amino acids in length . . . For example, in one variation, the peptides are formed with terminal cysteines which can be made to form an intramolecular disulfide bond. Thus, in one preferred embodiment, the peptide further comprises amino- and carboxy-terminal cysteine residues.

The above passage clearly describes peptides having more than eight amino acids, e.g., peptides having 100, 99, or 97 amino acids, and comprising N- and C-terminal cysteine residues. The Office has provided no reasoning to the contrary. The subject matter of claims 2 and 23 is clearly described in the specification, and the rejection should be withdrawn.

V. The Indefiniteness Rejection Under 35 U.S.C. § 112, Second Paragraph, Should be Withdrawn

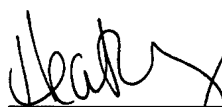
The Office rejected claim 36 for lack of antecedent basis for "monomers."
The rejection is moot in light of the amendment to claim 36.

VII. Conclusion

For the reasons given above, Applicants submit that the claims are in condition for allowance and request expedited notice of the same.

Dated: October 31, 2007

Respectfully submitted,



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I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the U.S. Postal Service as Express Mail, Airbill No. EL 995019653 US, on the date shown below in an envelope addressed to:
MS RCE Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: October 31, 2007

Signature: 

(Juan Quintero)

Docket No.: 28967/37084A
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Kari Alitalo et al.

Application No.: 10/046,922

Confirmation No.: 3363

Filed: January 15, 2002

Art Unit: 1644

For: VEGFR-3 INHIBITOR MATERIALS AND
METHODS

Examiner: P. N. Huynh

REQUEST FOR SUSPENSION OF ACTION

MS RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicant hereby requests that action by the U.S. Patent and Trademark Office be suspended on the above-identified patent application for a period of three months. This request is filed with a Request for Continued Examination (RCE) under 37 CFR 1.114.

Our check in the amount of \$130.00 covering the fee set forth in 37 CFR 1.17(i) is enclosed. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 13-2855, under Order No. 28967/37084A. A duplicate copy of this paper is enclosed.

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Accordingly, it is respectfully requested that this request for suspension of action be granted.

Dated: October 31, 2007

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